Mechanism and Utility of Direct Neuronal Conversion with a MicroRNA-Chromatin Switch

Grant Award Details

Mechanism and Utility of Direct Neuronal Conversion with a MicroRNA-Chromatin Switch

Grant Type: Basic Biology IV

Grant Number: RB4-05886

Project Objective: The PI has previously discovered that fibroblasts can be converted to neurons through recapitulation of a developmental, miRNA-chromatin switch involving cell-type specific remodeling of the ATP-dependent BAF complex. The goals of this project are to define the relationship between the miRNA and neurogenic factors that cooperate in this process; to characterize the epigenetic state of induced neurons; to convert astrocytes and lymphocytes to neurons using similar principles; and to engineer a neuronal ground state that can be biased to produce different types of neurons.

Investigator:

Name:	Gerald Crabtree
Institution:	Stanford University
Type:	PI

Disease Focus: Neurological Disorders

Human Stem Cell Use: Directly Reprogrammed Cell

Award Value: $1,392,150

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Mechanism and Utility of Direct Neuronal Conversion with a MicroRNA-Chromatin Switch

Public Abstract: Many human diseases and injuries that affect the brain and nervous system could potentially be treated by either introducing healthy neurons or persuading the cells that normally provide supporting functions to become functioning neurons. A number of barriers must be traversed to bring these goals to practical therapies. Recently our laboratory and others have found ways of converting different human cell types to functioning neurons. Surprisingly, two routes for the production of neurons have been discovered. Our preliminary evidence indicates that these two routes are likely to work together and therefore more effective ways of producing neurons can likely be provided by understanding these two routes, which is one aim of this application. Another barrier to effective treatment of human neurologic diseases has been the inability to develop good models of human neurologic disease due to inability to sample tissues from patients with these diseases. Hence we will understand ways of making neurons from blood cells and other cells, which can be easily obtained from patients with little or no risk. Our third goal will be to understand how different types of neurons can be produced from patient cells. We would also like to understand the barriers and check points that keep one type of cell from becoming another another type of cell. Understanding these mysterious processes could help provide new sources of human cells for replacement therapies and disease models.

Statement of Benefit to California: The state of California and its citizens are likely to benefit from the work described in this proposal by the development of more accurate models for the testing of drugs and new means of treatment of human neurologic diseases. Presently these diseases are among the most common afflicting Californians, as well as others and will become more common in an aging population. Common and devastating diseases such as Alzheimer's, Schizophrenia, Parkinson's Disease, and others lack facile cell culture models that allow one to probe the basis of the disease and to test therapies safely and without risk to the patient. Our work is already providing these models, but we hope to make even better ones by understanding the fundamental processes that allow one cell type (such as a skin cell or blood cell) to be converted to human neurons, where the disease process can be investigated. In the past the inability to make neurons from patients with specific diseases has been a major roadblock to treatment. In the future the studies described here might be able to provide healthy neurons to replace ones loss through disease or injury.